PATENT SPECIFICATION

NO DRAWINGS

907,309

Date of Application and filing Complete Specification: Feb. 16, 1960.

No. 5482/60.

Application made in United States of America (No. 793,945) on Feb. 18. 1959.

Complete Specification Published: Oct. 3, 1962.

Index at acceptance:—Classes 81(1), B6; and 2(6), P8C(2:6A:8B:10:13A:14B:20B:20C: 20D2), P8D(1B:2A:2B2).

ERRATA

SPECIFICATION NO. 907,309

Page 1, line 20, *for* "are" *read* "art"

Page 1, line 42, *for* "cyrup" *read* "syrup"

Page 1, line 74, *for* "phthale" *read* "phthalate"

Page 2, line 54, *delete* "oil"

Page 2, line 67, *for* "plasticizing" *read* "polishing"

Page 4, line 11, *for* "of" *read* "or"

Page 8, line 6, *for* "Form" *read* "From"

THE PATENT OFFICE,
12th February, 1963

DS 70710/1(5)/R.109 200 2/63 PL

num.

In the tablet coating are it is a well known procedure to first coat a compressed pellet or tablet with a water repellent resinous material such as zein or shellac which is used to protect the tablet from moisture later applied. Next are applied the sub-coating materials such as gelatin and acacia along with dusting of the sub-coating with powders especially designed for this purpose and known as sub-coating powders. This sub-coating procedure is required in the normal tablet coating art because a bare, compressed tablet usually has sharp edges which will not take a subsequent sugar coat evenly in the same amount as will be deposited on the surfaces of the tablet and will leave weak spots in the coating. Sub-coating is applied in order to round the corners and convert the tablet into more or less of an oval shaped object without sharp corners. Then a coating of heavy syrup with color added is usually applied over the sub-coat and numerous individual layers of this heavy cyrup coating with color are applied. Usually a sub-coating powder is suspended in the heavy syrup coating composition prior to its aplication. Finally several coats of a heavy syrup coating with color are put on top of considerably to the cost of a suitable tablet.

In our own prior U.K. Specifications Nos. 762,229 and 764,342 there is described a composition for coating tablets which comprises a hard water soluble or water dispersible component (which is wax or wax-like substance) and a film forming substance. Suitable film forming substances which are disclosed in the said Specifications include cellulose acetate phthale, phthalic glyceride condensation products, polyvinyl acetate and a glyptal resin prepared by copolymerisation of phthalic anhydride, glycerol and stearic acid under controlled conditions.

It has now been discovered that particularly suitable substances for forming a thin plastic film which is also substantially water permeable are the polymers and copolymers of lower alkylmethacrylates.

According to the present invention there is now provided a coated solid medicament having as the coating material a film of a physiologically acceptable composition consisting essentially of the water permeable combination of a water soluble wax as herein defined and a polymeric substance comprising a poly-loweralkyl-methacrylate, a copolymer of a lower alkylacrylate with a loweralkylmeth-

[*Price 4s. 6d.*]

Price 5s. 0d.

Price 25p

Price 75

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International Classification:—A61k. C08f.

COMPLETE SPECIFICATION

Water Permeable Tablet Coating and method of application

We, ABBOTT LABORATORIES, a Corporation organized and existing under the laws of the State of Illinois, United States of America, of 14th Street, and Sheridan Road, North Chicago, County of Lake, State of Illinois, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to tablets and other individual dosage forms which are characterized by a thin film coating of a water permeable plastic composition, and to the method of making such tablets and dosage forms. The invention also relates to a thin water permeable tablet coating film, and to a liquid composition useful for laying down the aforementioned film.

In the tablet coating are it is a well known procedure to first coat a compressed pellet or tablet with a water repellent resinous material such as zein or shellac which is used to protect the tablet from moisture later applied. Next are applied the sub-coating materials such as gelatin and acacia along with dusting of the sub-coating with powders especially designed for this purpose and known as sub-coating powders. This sub-coating procedure is required in the normal tablet coating art because a bare, compressed tablet usually has sharp edges which will not take a subsequent sugar coat evenly in the same amount as will be deposited on the surfaces of the tablet and will leave weak spots in the coating. Sub-coating is applied in order to round the corners and convert the tablet into more or less of an oval shaped object without sharp corners. Then a coating of heavy syrup with color added is usually applied over the sub-coat and numerous individual layers of this heavy cyrup coating with color are applied. Usually a sub-coating powder is suspended in the heavy syrup coating composition prior to its aplication. Finally several coats of a heavy syrup coating with color are put on top of the previously applied coats and then a thin syrup coating is applied over the entire mass. Finally it is desirable to employ a polishing operation such as for instance, the application of a wax to the coated tablet. The result is a substantially oval shaped coated tablet having no sharp corners and characterized by pleasing appearance and taste. Tablet coating is, however, quiet an expensive operation and requires from four to six days for the complete application and polishing of the tablet. The long time is required because the syrups and the sub-coats are put on from aqueous solution or suspension and between each coat it is necessary to rotate the tablets vigorously in a coating pan with air blowing over the tablets in order to evaporate the moisture and form a hard dry coat. It is recognized that coating adds considerably to the cost of a suitable tablet.

In our own prior U.K. Specifications Nos. 762,229 and 764,342 there is described a composition for coating tablets which comprises a hard water soluble or water dispersible component (which is wax or wax-like substance) and a film forming substance. Suitable film forming substances which are disclosed in the said Specifications include cellulose acetate phthale, phthalic glyceride condensation products, polyvinyl acetate and a glyptal resin prepared by copolymerisation of phthalic anhydride, glycerol and stearic acid under controlled conditions.

It has now been discovered that particularly suitable substances for forming a thin plastic film which is also substantially water permeable are the polymers and copolymers of lower alkylmethacrylates.

According to the present invention there is now provided a coated solid medicament having as the coating material a film of a physiologically acceptable composition consisting essentially of the water permeable combination of a water soluble wax as herein defined and a polymeric substance comprising a poly-loweralkyl-methacrylate, a copolymer of a lower alkylacrylate with a loweralkylmeth-

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acrylate, or a copolymer of a loweralkylmethacrylate with methacrylic acid. Several other ingredients may be added to the previously named ingredients in order to enhance the properties of the coating obtained from the composition. Among the more important of these additional materials are colouring materials, water insoluble waxes such as beeswax and paraffin which are glossing and polishing agents, plasticizing agents, and possible surface active agents, anti-sticking agents and drying oils.

The term "water soluble wax" as used herein means a water-soluble wax of the polyethylene glycol type having a melting point of at least 50°C, and also water dispersible waxes such as glyceryl monostearate and diglycol stearate which may be used either alone or in addition to the water soluble polyethylene glycol. The polymers employed are loweralkylmethacrylate polymers and also the copolymers of loweralkylacrylates with loweralkylmethacrylates or the copolymers of loweralkylmethacrylates and methacrylic acid. Such copolymers may contain from 70% to 95% by weight of loweralkylacrylate or loweralkylmethacrylate. Suitable plastics include methylmethacrylate, ethylmethacrylate, methylacrylate, ethylacrylate, copolymers of methylmethacrylate and methylacrylic acid as well as methylacrylate-methylmethacrylate copolymers. (By the term "loweralkyl-" is intended an alkyl group having from 1 to 4 carbon atoms).

Among the coloring agents which may be used in the practice of this invention are any of the non-toxic dyes, lakes and pigments which have been certified for use in the food, drug and cosmetic industries. For example, we have found that dyes of the type represented by red D & C #37 green F. D. & C. #1, yellow D & C #11, red D & C #21, orange D & C #4, red D & C #18 and red D & C #39 are suitable for use as colorants in the coating composition. Among the pigments which we have found suitable are yellow hydrated iron oxide, brown hydrated iron oxide, red iron oxide, black iron oxide, titanium dioxide, and the ultramarine blues. Many lakes are found suitable in the practice of this invention and D. & C. red #3, D. & C. orange #17, D. & C. green #1, D. & C. red #1, D. & C. yellow #1 are representative of the class. A lake is a dye which has been precipitated on an oil insoluble metallic compound. In the case D. & C. dyes, which means those suitable for use in the drug and cosmetic industry, it is necessary to deposit the dye on a pharmaceutically acceptable carrier such as aluminum hydroxide.

Among the water insoluble waxes used as glossing and polishing agents which we have found suitable are beeswax, lanolin, stearic acid, cocoa butter and cetyl alcohol. For plasticizing agents we may use castor oil, mineral oil, corn oil, sesame oil and propylene glycol. If desired, we may also substitute for the plasticizing agent a portion of a drying oil such as soy bean oil and we also may use surface active agents such as the polyoxyethylene sorbitan derivatives and the sulfated fatty alcohols of the Duponol type.

When the foregoing composition is applied to tablets in the manner which we recommend as part of our invention it is possible to provide a suitable coating for a tablet or the like with the use of a relatively few coats or applications of the coating material. A highly important advantage of this invention is that the coating composition described herein can be applied from solution in a non-aqueous solvent for the wax and the polymer or copolymer such as acetone, alcohol or a mixture thereof, and as a result the drying time between coats is reduced from approximately an hour or two in the case of water down to about 5 minutes in the case of the solvent solution. Hence, it is possible to completely coat a tablet in a matter of minutes where prior practices have required four to six days to obtain a suitable coating.

When the coating composition claimed herein is applied without coloring agent a pleasing white tablet is obtained. The white coating may be rendered opaque by the addition of a quantity of titanium dioxide for example, if desired. The invention is most highly suitable, however, to the application of colored film coatings of the type described in which a small quantity of a suitable coloring agent such as the dyes, lakes and pigments previously set forth are incorporated into the solution prior to application on the tablets. In this manner a highly pleasing appearance is given to the tablets and the tablets may be regarded as "elegant" in the terms of the trade. A tablet coated according to the practice of this invention is considerably smaller in size than one coated by the initially described standard procedure and the smaller tablet is more acceptable because it can be swallowed more easily. The film of this invention very effectively coats the tablets so that no unpleasant taste can be perceived but at the same time distinctive markings punched into the tablet core will show through very clearly and be readily discernible on the surface. Since no sugar coating is required in order to give these tablets elegance the taste appeal to children may be overcome and the chance of accidental ingestion of the tablets is substantially minimized. Also, the absence of sugar is a distinct advantage in those instance where it is desirable to limit caloric intake. A sweetening or flavoring agent may be added of course, if desired.

We prefer to use between about 10 to 25 parts by weight of the water soluble wax per 100 ml. of the ultimate fluid coating composition for application to tablets. Likewise, we may use between about 5 and about 12 parts

by weight of the loweralkylmethacrylate polymer or copolymer per 100 ml. of ultimate fluid coating composition. The waxy adjuvant is used in an amount not greater than 1 gram and the plasticizing agent is used in an amount not greater than 2 grams per 100 ml. of ultimate mixture.

In the finished dry coating on the tablet we use about 10 to 25 parts by weight of the water soluble wax to about 5 to 12 parts by weight of the polymer or copolymer, preferably between about 45% and about 83% by weight of the water-soluble wax to between about 17% and about 55% by weight of the loweralkylmethacrylate polymer or copolymer. The per cent by weight of additives such as colorants, plasticizers and waxy adjuvants is quite small and usually does not exceed 5% by weight in total amount.

The following examples are presented in order to describe the invention more fully but it should be understood that the invention is not intended in any way to be limited by the examples.

EXAMPLE I

A tablet coating solution is made up according to the following formula:

Polyethylene glycol—6000	10.0 g.
Methylmethacrylate-methacrylic acid copolymer	5.0 g.
Ethanol	15 cc.
Acetone q.s. to	100 cc.

The polyethylene glycol and copolymer are dissolved in warm acetone and ethanol and the mixture is thoroughly stirred. The solution is applied to a moving bed of tablets or granules by pouring small portions onto the tablets. As the tablets rotate the material is distributed evenly over the surface thereof and in a few minutes time the solvents will have evaporated leaving a dry hard film. Thereafter, a second coat is applied in the same manner and subsequent coats are applied until a film of the desired thickness is obtained. Tablets coated in this manner are pleasing in appearance and will disintegrate without delay either in water or in gastric secretions. The disintegration of the tablet may be speeded up somewhat by incorporating into the tablet one of the well-known disintegrators.

EXAMPLE II

A solution suitable for coating tablets is prepared according to the following formula:

Polyethylene glycol—6000	14.0 g.
Methylmethacrylate-methacrylic acid copolymer	6.0 g.
Yellow dye D. & C. #11	0.5 g.
Methanol	20 cc.
Acetone q.s. to	500 cc.

The formula is made up the same way as in Example I except the yellow dye is added to a portion of the acetone and methanol prior to thorough mixing of the solution. Tablets coated with 10—20 coats of this solution give a very pleasing yellow appearance and are much smaller and easier to swallow than a similar tablet which has undergone sub-coating and sugar coating in the normal tableting procedure.

EXAMPLE III

A solution suitable for use in coating tablets is prepared according to the following formula:

Polyethylene glycol—6000	22.5 g.
Methylmethacrylate-methacrylic acid copolymer	7.5 g.
Castor oil	1.25 g.
Acetone q.s. to	100 cc.

This solution is made up in the same manner as previously described and is applied to tablets in the same way. The film applies to the tablet quite evenly with a suitable distribution of film on the sides, edges and faces of the tablet. A few coats of the foregoing solution will give a film of approximately 0.005 inch in thickness and provides a suitable pleasing film about the tablet core.

EXAMPLE IV

A solution for use in coating tablets of the like is prepared according to the following formula:

Polyethylene glycol—4000	20.0 g.
Methylmethacrylate-methacrylic acid copolymer	7.0 g.
Vinyl stearate	1.0 g.
Acetone q.s. to	100 cc.

This solution is prepared similarly to the preceding solutions. The vinyl stearate is employed as an antisticking agent. The film obtained is quite smooth and even and deposits uniformly on the sides, edges and faces of the tablet.

EXAMPLE V

A preferred solution suitable for application to tablets to form a thin film thereon was made up according to the following formula:

Polyethylene glycol—6000	14.0 g.
Methylmethacrylate polymer	6.0 g.
Yellow dye, D. & C. #11	0.5 g.
Castor oil	1.25 g.
Stearic acid	1.0 g.
Acetone q.s. to	100 cc.

The polyethylene glycol and the stearic acid are added to warm acetone and when the acetone has cooled somewhat the yellow dye and castor oil are also added. The entire solution is mixed with the methylmethacrylate and thereafter applied to tumbling tablets in customary tablet coating procedures. For instance about 10 cc. of the solution may be applied to about 2000 tablets in a rotating pan and after about 5 minutes the coat will be evenly distributed on all of the tablets and will be substantially dry. Thereafter another 10 cc. portion may be applied and the procedure repeated a number of times until a coating of suitable thickness has been established.

EXAMPLE VI

A solution suitable for application to tablets and the like to form a thin film thereon is made up according to the following formula:

Polyethylene glycol—6000	12.0 g.
Methylmethacrylate polymer	5.0 g.
Red dye, D. & C. #37	100 mg.
Corn oil	1.25 g.
Cocoa butter	1.0 g.
Acetone q.s. to	100 cc.

The solution is prepared in the manner previously set forth in Example V and is applied to tumbling tablets in the same way.

EXAMPLE VII

A solution suitable for application to tablets and the like to form a thin film thereon is made up according to the following formula:

Polyethylene glycol—6000	28.0 g.
Methylmethacrylate polymer	12.0 g.
Green dye, D. & C. # 1	2.0 g.
Mineral oil	1.25 g.
Lanolin	1.0 g.
Acetone q.s. to	100 cc.

This solution is prepared in the same manneras set forth in the preceding examples.

EXAMPLE VIII

A solution suitable for application to tablets and the like to form a thin film thereon is made up according to the following formula:

Polyethylene glycol—6000	8.0 g.
Methylacrylate-methylmethacrylate copolymer	16.0 g.
Orange dye, D. & C. # 4	250 mg.
Orange lake, D. & C. # 17	2.0 g.
Propylene glycol	1.25 g.
Ethyl acetate	5 cc.
Methyl ethyl ketone q.s. to	100 cc.

The solution is made up in the same manner as set forth in the previous examples. It differs therefrom in that a portion of orange lake is substituted for a portion of dye in order to provide greater depth of color and superior covering power for the colorant in the solution.

EXAMPLE IX

A solution suitable for application to tablets to form a thin film thereon is made up according to the following formula:

Polyethylene glycol—6000	10.0 g.
Methylacrylate-methylmethacrylate copolymer	25.0 g.
Yellow lake, D. & C. # 1	15.0 g.
Methanol	20 cc.
Paraffin	1.0 g.
Acetone q.s. to	100 cc.

The solution is prepared in the same manner as set forth in the previous examples and is applied to tablets in the same way. The lake employed in this example gives a brilliant color and has excellent covering qualities for the tablet core. Lakes are quite useful in covering up tablets which have an off color or a mottled appearance.

EXAMPLE X

A solution suitable for application to tablets to form a thin film thereon is made up according to the following formula:

Polyethylene glycol—6000	12.0 g.
Methylacrylate-methylmethacrylate copolymer	5.0 g.
Red lake, D. & C. # 3	6.0 g.
Castor oil	1.25 g.
Acetone q.s. to	100 cc.

This solution is made up in a manner similar to as set forth in the previous examples and when applied to tablets is found to provide a pleasing red color which has strong covering properties.

EXAMPLE XI

The formula in Example X was duplicated substituting 3 grams of red iron oxide pigment for the lake of the previous example. In this example a dull red color is obtained when the solution is applied to the tablets and the covering power of the solution is very good.

EXAMPLE XII

A solution suitable for application to tablets and the like to form a thin film thereon was made up according to the following formula:

Glyceryl monostearate	14.0 g.
Methylacrylate-methylmethacrylate copolymer	6.0 g.
Methanol	20 cc.
Acetone q.s. to	100 cc.

This solution is made up in a manner similar to that previously set forth and is applied to tablets in a similar fashion. If desired we may also add a colorant, a plasticizer and a wax as in the previous examples. While glyceryl monostearate is not water soluble it is water dispersible in the concentrations used herein and particularly in combination with the plastic material. Tablets coated with a film of the foregoing solution will disintegrate readily in water or in gastric secretions.

EXAMPLE XIII

A solution suitable for application to tablets to form a thin film thereon is made up according to the following formula:

Polyethylene glycol—6000	20.0 g.
Ethylmethacrylate polymer	10.0 g.
Titanium dioxide	3.0 g.
Acetone q.s. to	100 cc.

A solution is made up in the manner previously described and may also have colorant, plasticizer and wax added thereto if desired. The titanium dioxide is employed herein as an opaquing agent.

Form the foregoing discussion of the invention it will be clear that we have provided a novel and highly unusual coating for tablets. It does away with the long and involved coating and drying procedure normally used in the tablet coating art. The film is uniformly thin on the tablets and provides all of the necessary protection and elegance that can be obtained in any other tablet coating procedure. In essence, this invention makes possible the substitution of a single thin film on tablets for the previously known massive sub-coating and sugar coating thereon.

WHAT WE CLAIM IS:—

1. A coated solid medicament having as the coating material a film of a physiologically acceptable composition consisting essentially of the water permeable combination of a water soluble wax as herein defined and a polymeric substance comprising a poly-loweralkyl-methacrylate, a copolymer of a loweralkylacrylate with a loweralkylmethacrylate, or a copolymer of a loweralkylmethacrylate with methacrylic acid.

2. A coated solid medicament as claimed in claim 1 wherein the water soluble wax is present in a proportion of about 10 to 25 parts by weight to about 5 to 12 parts by weight of the polymeric substance.

3. A coated solid medicament as claimed in claim 2 which is in the form of a tablet and wherein the water soluble wax is a polyethylene glycol having a melting point of at least 50°C. and the polymeric substance is polymethylmethacrylate.

4. A coated solid medicament as claimed in claim 2 which is in the form of a tablet and wherein the water soluble wax is a polyethylene glycol having a melting point of at least 50°C. and the polymeric substances is methylmethachylate-methacrylic acid copolymer.

5. A coated solid medicament as claimed in claim 2 which is in the form of a tablet and wherein the water soluble wax is a polyethylene glycol having a melting point of at least 50°C. and the polymeric substance is methylacrylate-methylmethacrylate.

6. A method of coating tablets and the like which comprises applying to the said tablets a film coating of a physiologically acceptable fluid coating composition consisting essentially of the water permeable combination of a water soluble wax as herein defined and a polymeric substance comprising a poly-loweralkylmethacrylate, a copolymer of a loweralkylacrylate with a loweralkylmethacrylate, or a copolymer of a loweralkylmethacrylate with methacrylic acid in a non-aqueous solvent for said wax and said polymeric substance.

7. A method of coating a solid medicament as claimed in claim 6 wherein the water soluble wax is present in a proportion of about 10 to 25 parts by weight and the polymeric substance is present in a proportion of about 5 to 12 parts by weight based on the weight of 100 mls. of the fluid composition.

8. A method as claimed in claim 7 wherein the medicament is a tablet and the water soluble wax is polyethylene glycol having a melting point of at least 50°C.

9. A method according to claim 8 wherein the polymeric substance is polymethylmethacrylate.

10. A method according to claim 8 wherein the polymeric substance is methylmethacrylate-methacrylic acid copolymer.

11. A method according to claim 8 wherein the polymeric substance is methylacrylate-methylmethacrylate copolymer.

12. A fluid composition adapted for application to tablets and the like as a film coating thereon which consists essentially of about 10 to 25 parts by weight of a water soluble wax as herein defined, about 5 to 12 parts by weight of a polymeric substance comprising a poly-loweralkyl-methacrylate, a copolymer of a loweralkylacrylate with a loweralkylmethacrylate, or a copolymer of a loweralkylmethacrylate with methacrylic acid and a non-aqueous solvent for said wax and said polymeric substance, based on the weight of 100 ml of ultimate composition.

13. A fluid composition as claimed in claim 7 wherein the water soluble wax is a polyethylene glycol having a melting point of at least 50°C.

14. A coated solid medicament having as the coating material a film of a physiologically acceptable composition substantially as herein described with reference to any one of Examples I to XIII.

15. The method of coating tablets and the like substantially as herein described with reference to any one of Examples I to XIII.

16. A fluid composition adapted for application to tablets and the like substantially as herein described with reference to any one of Examples I to XIII.

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